

From: [Bill Jacobs](#)  
To: [John Hebert](#); [Hal.Ambuter@reckittbenckiser.com](mailto:Hal.Ambuter@reckittbenckiser.com)  
Cc: [Jennifer Gaines](#); [Dan Peacock](#)  
Subject: Re: Fw: Rodenticide Question from RB  
Date: 04/09/2009 02:31 PM

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What appears in advertising for others' products may or may not have been reviewed and accepted by EPA. Such claims are not necessarily valid and should not be regarded as guidance for other products.

Claims regarding how many rodents a given amount of bait could be expected to kill are NOT based upon LD50 information. Half of the mice administered an LD50 dosage would be expected to survive.

LD50 data are derived from oral-gavage trials and often are poor predictors of how a rodenticide performs when administered in bait form. Cholecalciferol tends to be more toxic in bait form than would be predicted from published LD50 figures. First-generation anticoagulants have relatively high acute oral LD50 figures but much lower 5-day subchronic LD50s (Ashton, *et al*, 1987, in: Richards, C.G.L. and Ku, T.Y., eds., *Control of Mammal Pests*, Taylor & Francis, London, pp. 187-197). With the second-generation anticoagulants, there tends to be less disparity between acute oral and 5-day subchronic LD50s. The differences among anticoagulants probably are due to the relative affinities of Vitamin-K "receptors" for the various compounds.

How many rodents a given amount of bait could kill in theory and how many that amount reasonably could be expected to kill are different matters. Label claims should only be based upon reasonable expectations which, in turn, are based upon several considerations.

Laboratory efficacy trials with house mice typically are run with group-caged test groups of laboratory strain mice. Under such conditions, groups of 5 or 10 mice are confined in a small area with only 2 foods offered -- the toxic bait and OPP challenge diet. Depending upon the quality of the lab work, the calculated amounts of those substances consumed by mice could be exaggerated or under-recorded, although protocol stipulations should limit inaccuracy. The mice may consume the rodenticide by eating the bait, via coprophagy, and/or through cannibalism. Thus, some poison molecules could be involved in dosing more than one mouse. Under such artificial circumstances, a given amount of bait would be likely to be able to kill more mice than it reasonably could be expected to kill under conditions of actual use.

Actual use involves baiting wild-type house mice in areas that typically are much larger and structurally much more complicated than a test cage. Home ranges for individual mice typically are relatively small, sometimes extending not much more than a dozen feet in any direction. Depending upon factors such as population density and kinship, house mouse societies may be organized territorially or as within-sex dominance hierarchies. Either way, not every mouse will have equal access to every place in the infested area, especially at the onset of baiting, before individuals start to weaken and die. Mice also tend to nibble small amounts of food from multiple locations in their home range rather than feeding heavily from one location (which is more typical of commensal rats). For that reason, labels call for multiple bait placements at intervals of 8 to 12 feet in infested areas.

Under conditions of actual use, the number of mice exposed to a given quantity of

bait will be affected by the number of bait placements that quantity affords and the number of mice that have access to those placements. A 1.5-oz quantity of bait would be sufficient for 3-6 placements at the rate of 1/4-1/2 oz per typical placement that has been prescribed for decades for anticoagulant baits that are sold "loose" (i.e., not in placepacks or discrete bait blocks). However, 1.5 oz of bait sold as a block, in a placepack, or in Mouse Prufe II would allow for only one placement according to the use directions that such products typically have. In mouse-only field trials conducted prior to the initial U.S. registration of Brodifacoum, more than 1/2 oz of bait had been taken from some placement loci when they were revisited 24 hours after bait placement, but consumption was less than 1/2 oz at 80% of the loci 72 hours (3 days) after placement and at 50% of the loci 144 hours (6 days) after placement. On the basis of such data, placement amounts of up to 2 oz were permitted for controlling house mice but only at points of very high mouse activity. As bait consumption by individual mice likely was on the order of a few grams/day, more than one mouse likely was involved in removing bait from the loci from which >1/2 oz disappeared rapidly, although some of the bait removed might have been cached and not consumed at the placement site.

Label statements regarding the numbers of commensal rats that a given package size of bait could be expected to kill arose out of a need to qualify rat claims for packages that contained less than 16 oz of bait, which is the maximum single-placement amount that labels for anticoagulant baits prescribe when commensal rats are being targeted. Without a qualifying statement, the claim "KILLS RATS" would be somewhat misleading. Qualifying statements for rats typically present a range in numbers of rats that a given quantity of bait could be expected to control. For example, 4 oz of bait -- the minimum placement size for rats prescribed on labels for many anticoagulant bait products -- could be consumed by a single rat, assuming that the bait were fed on almost exclusively by that animal for 4 pre-symptomatic days at the proverbial rate of an ounce of grain a day. That rationale sets the lower end of the qualifying statement at one rat. Alternatively, several rats might have access to the bait and might remove all or most of the 4 oz in one day. The more rats that access the bait and the more equitably it is "shared", the less likely that any of them would be fatally poisoned by the limited amount offered. Equitable sharing is not expected with rats; but it is reasonable to conclude that the first rat that feeds on the bait would leave enough behind to kill perhaps 2 more rats, provided that the food source was not defended at the locus or removed to a burrow or other nesting location. Thus, the qualifying statement for rats for a 4-oz package would read something like "The amount of bait in this package would not be expected to kill more than 1 to 3 rats."

With house mice, the packages in commerce contain 1/2 oz of bait or more, equalling or exceeding the maximum rate for one typical placement. Consequently, qualifying statements regarding house mouse claims do not appear on product labels. Instead, claims regarding how many mice a given quantity of bait might kill usually are framed as boasts about the product's potential efficacy. Such claims have to be monitored and based upon a consistent rationale as registrants may try to one-up one another. Dividing the amount of poison in a given quantity of bait (e.g., 1 mg in 20 g of a 0.005% a.i. product) by the product of an LD50 figure and the weight of a typical mouse would yield a relatively large quotient which would be false or misleading for the reasons noted above. Using the total bait consumption figures from a laboratory efficacy trial and dividing that by the number of test-group subjects killed could give an optimistic figure regarding the numbers of mice that the amount in a package could kill, especially if the package afforded only one

placement location at a time.

The appropriate way to have a claim like "This package contains enough bait to kill up to X mice" accepted is to propose it formally, provide a rationale for it (not involving LD50s), and supply whatever data you have that bear upon the issue. We then could review your proposal in the context of your submission and any other actions that we might have taken involving the same type of claims for similar products. Note that accepted claims will not necessarily be similar among products and active ingredients due to differences in package size and modes of action.

▼ John Hebert---04/09/2009 10:45:49 AM---Bill - Can you please take a look at the following email. Don't we base the number of mice that a b

From: John Hebert/DC/USEPA/US  
To: Bill Jacobs/DC/USEPA/US@EPA  
Cc: Jennifer Gaines/DC/USEPA/US@EPA  
Date: 04/09/2009 10:45 AM  
Subject: Fw: Rodenticide Question from RB

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Bill - Can you please take a look at the following email. Don't we base the number of mice that a bait/product can kill on the minimum placement size of .5 oz? I guess this is based on the LD50 of the ai; but is this only for second generation ais? thanks.

john

-----Forwarded by John Hebert/DC/USEPA/US on 04/09/2009 10:40AM  
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To: Jennifer Gaines/DC/USEPA/US@EPA, John Hebert/DC/USEPA/US@EPA  
From: "Ambuter, Hal" <Hal.Ambuter@reckittbenckiser.com>  
Date: 04/01/2009 09:27AM  
Subject: Rodenticide Question from RB

Jennifer/John

Our Marketing people have seen some new claims on competitive products listing the amount of mice that a product can kill

for example